Review paper

Restoring sinus rhythm in patients at a high risk for postoperative atrial fibrillation

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Abstract

The development of atrial fibrillation (AF) is one of the most common occurrences during follow-up after cardiac surgery. AF is a well recognized risk factor for increased postoperative complications and mortality. Preoperative use of antiarrhythmic medications has also been associated with a higher rate of postoperative AF. To enhance postoperative recovery of sinus rhythm in these patients, various perioperative antiarrhythmic drug regimens, including amiodarone, and repeated DC shock cardioversion have been adopted. Despite such strategies, AF tends to re-establish itself after surgery in over 75% of patients, with patients having mitral surgery faring worse than those undergoing aortic valve operations. The development of surgical ablation enables sinus rhythm to be restored in as many as 70% of patients. However, the large scale adoption of such techniques has also raised the issue of post-ablation arrhythmias. Although relapsing atrial fibrillation is generally addressed conservatively, most automatic arrhythmias require electrophysiological assessment and ablation, frequently transseptal. Completeness of the lesion sets and durable transmurality of the ablations are key to preventing most postoperative dysrhythmias.

Key words: ablation, atrial fibrillation, cardiac surgery, sinus rhythm.

Introduction

The development of atrial fibrillation is one of the most common occurrences during follow-up after cardiac surgery. Atrial fibrillation is a well recognized risk factor for increased mortality in the general population [1]. Likewise, in patients undergoing mitral surgery, persistent postoperative AF has been associated with poorer long-term survival [2, 3]. Additionally, an irregular heartbeat may frequently cause patients discomfort and anxiety, and loss of synchronous atrio-ventricular contraction may compromise haemodynamics [4]. Finally, the detrimental effects of AF are even more pronounced in the presence of high ventricular rate, which can further worsen ventricular function in patients with an organic heart disease [5].

The recovery of stable sinus rhythm after surgery promotes better functional recovery [6], and dramatically increases the freedom from haemorrhagic and thromboembolic complications [4, 7], often allowing withdrawal of antiarrhythmic medications [8].

Among factors defining patients at a high risk for developing atrial fibrillation after open heart surgery are left atrial dilatation [2, 9, 10], older age [11], concomitant tricuspid procedures [3] and impaired left ventricular function [12, 13]. But undoubtedly, history of atrial fibrillation is by far the most potent predictor of postoperative persistent atrial fibrillation [2, 10, 12, 14]. Up to 50% of patients undergoing open heart surgery have had AF [10, 15-17].

The type and duration of preoperative atrial fibrillation are strong determinants of rhythm outcome. In patients undergoing mitral repair, Obadia et al. reported the likelihood of restoring sinus rhythm spontaneously after surgery to be as high as 80% when atrial fibrillation was intermittent or of less than one year duration [2]. The probability of return to sinus rhythm declined consistently for patients with atrial fibrillation lasting longer, and was less than 5% for an arrhythmia duration over 3 years [2]. In a similar series of patients undergoing valve surgery Jessurun et al. found the rate of spontaneous postoperative recovery of sinus rhythm at late follow-up to be 34% in patients with preoperative paroxysmal atrial fibrillation and only 4% in those with chronic atrial fibrillation [3]. It is generally accepted that patients with permanent atrial fibrillation lasting more than 6 months have less than 30% probability of recovering sinus rhythm spontaneously after surgery [2, 10, 18]. Among patients with history of atrial fibrillation concurrent risk factors such as older age, left atrial enlargement, left ventricular dysfunction, and increased pulmonary pressure further contribute to a lessening of the likelihood of sinus rhythm restoration in patients with preoperative atrial fibrillation [11-13, 19]. Preoperative use of antiarrhythmic medications has also been associated with a higher rate of postoperative atrial fibrillation [11].

To enhance postoperative recovery of sinus rhythm in these patients, various perioperative antiarrhythmic drug regimens, including amiodarone [3, 18] and repeated DC shock cardioversion, have been adopted [20]. Despite such strategies, atrial fibrillation tends to re-establish itself after surgery in over 75% of patients, with patients having mitral surgery faring worse than those undergoing aortic valve operations [20].

Surgical approaches to treat atrial fibrillation

Due to the incomplete understanding of the pathogenesis of atrial fibrillation there is no consensus on the ideal set of lines to be carried out during open heart surgery. The extent to which the origin of atrial fibrillation in the diverse settings relies more on focal activation or on re-entry circuits is still questioned [21]. Other possible mechanisms such as an altered tone of the autonomic nervous system possibly leading to substrate modification within the atrial wall have been advocated [22]. Due to the difficulties of performing an electrophysiological assessment intraoperatively, surgical approaches to atrial fibrillation have been traditionally anatomy-based.

The first approach aimed at restoring normal electrical and mechanical activity of both atria is the maze procedure, reported by Cox in 1991 and later modified [23, 24]. The maze operation consists in multiple incisions, prolonged by nitrous oxide cryoablation, up to the mitral and tricuspid annulus, in both atria, to interrupt all possible macroreentrant circuits. The pulmonary veins are isolated en bloc by a single box lesion. The incisions force the electrical activity of the atria to propagate from the sinus node to the atrioventricular node through narrow corridors of the atrial myocardium, providing electromechanical recruitment of both atria. In addition, the right and the left atrial appendages are resected.

Cox reported a success rate of 98% in a series of patients mainly affected by paroxysmal AF. Operative mortality was 2.5, and 25% of the patients required a permanent pacemaker [9]. Other groups have combined the maze procedure with other open heart procedures with a success rate varying between 70 and 96% [16, 22, 25, 26].

When the maze procedure is combined with other open-heart operations to treat chronic AF, operative morbidity is consistently increased [27, 28]. In this context the maze procedure significantly prolongs cardiopulmonary bypass and aortic cross clamp time and increases bleeding, blood product requirements and intubation time after operation [29].

In 1996, Harada et al. reported the constant finding of regular repetitive activation of the left atrium in patients with AF undergoing mitral valve surgery [30]. In the same year Sueda et al. documented in a similar series of patients shorter refractory periods leading to a shorter mean AF cycle length in the left atrium [31]. Both studies indicated that the left atrium was the driving chamber for AF, at least in patients with mitral valve disease. Such findings stimulated the search for simplified techniques limited to the left atrium to treat AF during mitral valve surgery.

Sueda called "simple left atrial procedure" a surgical encircling of the four pulmonary veins, connected to the mitral valve annulus by two cryoablation lines [31, 32]. The procedure was feasible in less than 30 min and SR was restored in 86% of patients.

In 2000 Kosakai reported the results of the Japanese Registry of AF surgery on over 2000 patients to show no significant difference among the results of a maze operation, a modified biatrial maze and Sueda's left approach [33].

All the different surgical ablation procedures performed in recent years include isolation of the pulmonary veins, either en bloc, with a single wide circle including all the posterior left atrium, or with two separate oval encirclings around the right and the left pulmonary vein couples, which are then connected with one or more additional ablations [34-36]. Exclusion of the left atrial appendage is also generally accepted [34-36]. Instead, the role of the connecting line to the mitral annulus (or left isthmus ablation) has been questioned. Some surgeons, in an attempt to simplify the operation, mainly due to concern about the risk of injuring a major coronary artery in the AV groove, reported omitting the mitral connecting lesion [37-39].

This nevertheless proved to lessen the atrial fibrillation cure rate considerably and to increase postoperative flutter [40, 41].

The role of adding the right sided lesions of the maze operation has been recently reconsidered after a recently reported extensive meta-analysis described better results in patients receiving a biatrial ablation approach, as opposed to those given a left ablation only, at all time intervals after surgery [42].

Latest developments

The advent of diverse physical means available for surgical ablation, allowing the creation of atrial scars without cutting and suturing, played a major role in stimulating the evolution of modern surgical approaches to atrial fibrillation.

In 1997, Melo reported the first use of endocardial radiofrequency in the open heart, to design 2 separate encircling lines around the left and the right pulmonary veins [43].

Following Sueda's experience, other groups reported performing a box-like lesion around all four pulmonary veins and a connecting lesion to the posterior mitral annulus using either cryoablation or unipolar radiofrequency with a 70 to 90% success rate [36, 44, 45].

In 1998, Rushat proved RF to be effective in an animal model even when ablations are performed from the epicardial surface [46].

In 2000 our group reported for the first time the use of epicardial RF ablation to perform a left atrial lesion set in a series of patients undergoing other cardiac operations [36].

The ablations were performed using a temperature-controlled unipolar linear RF catheter epicardially to isolate the pulmonary veins, and then endocardially to perform the connecting lines. This technique yielded a 75% SR maintenance rate at follow-up and allowed a significant shortening of cross-clamp time, thus allowing safer concomitant treatment of the arrhythmia [47].

In the new millennium there has been growing interest in epicardial ablation. Actually, all the recently introduced devices are devised to be used epicardially [48].

Also microwave proved suitable for epicardial ablation. Maessen reported promising results in a preliminary experience in 2002 [49]. Saltman et al. reported the feasibility of a thoracoscopic epicardial ablation approach using a specifically designed microwave probe [50]. Chitwood reported ablation with epicardial microwave and concomitant mitral surgery in patients undergoing robotic surgery [51].

Recently introduced argon cryothermy, which brings the tissue to much lower temperatures than nitrous oxide, has also been tested for epicardial ablation in the clinical setting [52, 53].

The latest device to be proposed in the beating heart ablation arena is high intensity focused ultrasound [54]. The introduction to clinical practice of laser technology is anticipated in 2008.

Besides shortening aortic cross-clamp time, epicardial ablation made atrial fibrillation surgery safer. During endocardial deployment, in fact, the ablation may spread outward beyond the atrial wall, thus exposing the surrounding structures (oesophagus, bronchial tree, phrenic nerves) to potential damage [55]. But despite clinical success in the range of 70-80%, all the above reported unipolar ablation devices share a common drawback: epicardial use on the beating heart does not generally grant transmurality [47, 56, 57].

Failure to penetrate has been related to the composition and to the thickness of the atrial wall [56]. The major obstacle to the progression of the lesion through the subendocardial layer is the convective cooling exerted by blood flowing through the atrial chamber.

Bipolar devices, first introduced into clinical practice in 2002 [58], were devised to obviate such problems. The clamping mechanism of bipolar devices, in fact, eliminates convective endocardial cooling and compresses the atrial walls, thus reducing tissue thickness and improving contact. Transmurality of bipolar radiofrequency atrial ablations has been proven both in the experimental [59] and in the clinical setting [58, 60, 61].

Another important aspect of bipolar ablation is the safety profile. In fact, during bipolar ablation, only the outer, inactive part of the clamp is in contact with the parietal pericardium so that only the tissue that is held between the jaws is consistently heated. Collateral damage of the structures surrounding the heart has not been reported with bipolar ablation to date. Furthermore, the time required for the ablation procedure is reduced to a few minutes.

Rhythm disturbances after ablation surgery

Early arrhythmias

Postoperative supraventricular arrhythmias occur in 35 to 60% of patients undergoing atrial fibrillation surgery [24, 36, 62]. Therefore, surgical ablation is the most arrhythmogenic context in cardiac surgery. Atrial fibrillation surgery shares with other cardiac surgery procedures the common risk factors for postoperative tachyarrhythmias: after cardiac surgery, arrhythmias are likely to occur because of the inflammatory effects of cardiopulmonary bypass [63-64] and myocardial ischaemia [65-66], due to atrial trauma related to atriotomies, as a consequence of postoperative pericarditis, and of the postoperative increase of adrenergic tone. These alterations lead to a temporary shortening of the refractory period of the atrial myocytes and to a dispersion of refractoriness, both favouring the formation of re-entrant circuits [67].

In addition to that, patients undergoing ablation surgery have larger atrial chambers and tend to be more frequently affected by valve disease, mostly involving the mitral valve [39, 47, 68]. Furthermore, the atrial myocardium in these patients is usually affected by varying degrees of structural derangement with cellular changes such as myocyte dedifferentiation and myocytolysis, and interstitial remodelling occurring preferentially in the posterior left atrial wall, in proximity with the confluence of the pulmonary veins [69, 70].

Finally, the evolution of the scar consequent to ablation is such that in the first days or weeks after the procedure, inflammatory processes are the main histological finding. It is not until 3 to 5 weeks after ablation that the lesion becomes a fibrotic scar [59, 71, 72].

The rationale for the use of antiarrhythmic medications after atrial fibrillation surgery was outlined for the first time by Cox in 1993 [73]. Exposing the results of his pioneering experience with the maze operation, the author documented early recurrences of supraventricular tachyarrhythmias as the most frequent postoperative complication, occurring in about one half of the patients. Cox described using a combination of digoxin and procainamide to deal with early (<3 months) rhythm instability.

Since then, all authors reporting results of any surgical procedure for atrial fibrillation have described the use of some combination of antiarrhythmic medications either for primary [32] or for secondary prevention [27] of postoperative recurrences, up to 3-6 months after operation [27-32].

Amiodarone, first proposed by our group in 2000 [36], is today used by most centres as the first choice drug for primary prevention of perioperative arrhythmias after ablation surgery [6, 18, 74-76]. I.V. amiodarone can easily be started during surgery and continued orally after recovery of peristalsis. The dosage is generally tapered to the individual patient's rhythm, to prevent an accentuation of post-ablation sinus node dysfunction [77, 78], or of AV block, possibly related to other aspects of the surgical procedure. Sotalol, beta-blockers or other medications are used as second choice drugs in the same context [49, 76, 79, 80]. Selective angiotensin II receptor antagonists such as irbesartan may further enhance the antiarrhythmic effect of amiodarone also in the postoperative course of ablation surgery [81].

Recently, a possible role for perioperative administration of corticosteroids has been hypothesized [82], but there is still no solid evidence supporting large scale adoption.

Early postoperative arrhythmias may occur in the form of atrial fibrillation, in more than 50% of the cases, as flutter or as mixed forms. They tend to occur in the first 10 days after surgery, with a peak on postoperative day 8 [65]. With optimization of medical treatment and hydroelectrolytic balance, these arrhythmias are generally self-terminating in the span of a few days, usually less than one week [65]. When needed, electrical cardioversion should be administered [47, 65, 83]. The timing of DC shock cardioversion is also a matter of debate. Generally, in the presence of a controlled heart rate and of stable clinical conditions it is desirable to postpone it until 10 to 14 days after surgery, since an excessively premature cardioversion early after the occurrence of arrhythmia is more likely to result in relapse and creates an improper distrust towards DC shock (which most of the time has been tried unsuccessfully also before surgery).

The specific set of lesions may influence early arrhythmias. A wide en bloc isolation of the posterior left atrium has been found to reduce early postoperative arrhythmias by a half with respect to separate isolation of the pulmonary veins as couples plus a linear connection [84]. This can be explained by a more effective exclusion of the ganglionic plexi of the heart, which have been implied in the determination of atrial arrhythmias, mainly by enhancing ectopic firing by the pulmonary veins [85]. Most of the ganglionic plexi are in fact located in the posterior left atrium [86].

It is noteworthy that early arrhythmias are not necessarily a marker of procedural failure. Perioperative rhythm disturbances have been correlated with late failure in most series [47, 76, 87]. But the consensus on the negative prognostic value of such arrhythmias is not unanimous [65]. Therefore repetitive attempts at DC shock conversion up to 3-6 months after surgery have been advocated [83].

Late arrhythmias

Among predictors of late failure, left atrial dilatation has been most frequently found to play a role [87-89] with a cut-off value of left atrial diameter ranging from 5 to 7 cm. A longer duration of atrial fibrillation has also been found to favour post-ablation relapse when late results are considered [88, 90, 91]. Low voltage of f waves [88], rheumatic heart disease [89], older age at surgery [47], rheumatic heart disease [89] and, arguably, concomitant ablation with respect to treatment of lone atrial fibrillation [87, 91] have also been found to negatively influence late results.

Operator dependant late arrhythmias depend on a variety of technical issues, most of which are related to the positioning and to the consistency of the ablation lines [92].

Left lesion sets have largely proven effective in dealing both with concomitant [31, 32, 36, 47] and with isolated [93] atrial fibrillation. A Japanese survey of atrial fibrillation surgery published in 2000 could show no difference among the follow-up results of the maze operation, a modified biatrial maze-like approach and a left atrial maze in a series of over 2000 patients undergoing concomitant ablation surgery [33]. Likewise, Deneke et al., in a comparative non-randomized study, demonstrated no significant difference in the rate of relapses between a left atrial and a biatrial approach performed with irrigated radiofrequency [94]. Conversely, a recently published extensive meta-analysis documented a better freedom from arrhythmia recurrence of biatrial approaches compared with left ablation alone at all time points after surgery [42]. Besides the issue of a higher efficacy towards AF relapse, omission of right lesions has been definitely correlated with a 2 to 7.5% rate of typical counterclockwise right flutter, frequently requiring further ablation after surgery [36, 95, 96].

The extent of left ablation is also important in the prevention of post-procedural arrhythmias. Isolation of the pulmonary veins is the mainstay of all currently used surgical procedures [31, 36-38, 60, 97]. The pulmonary veins can be isolated either en bloc or by means of two separate encircling lesions, then connected by one or more ablations. In the concomitant open heart ablation setting, the lesion connecting the isolated pulmonary veins with the posterior mitral annulus, also named the left isthmus lesion, plays a major curative role [98]. The omission of such a line has been related to a consistently increased higher rate of postoperative AF relapse in patients with preoperative permanent atrial fibrillation. Worse than that, a left atrial set of lesions lacking the mitral lesion has been associated with a close to 10% rate of atypical flutter [47].

Actually the key role of left atrial connecting lines was clearly pointed out in 2005 by Gaita and coworkers, whose randomized study demonstrated a complete set of left lines to grant much better late freedom from arrhythmias than pulmonary vein isolation alone [40].

Incomplete lesion sets may also result from gaps in the ablation lines. A direct cause-effect relationship between incomplete ablation lines and arrhythmia relapse has been clearly outlined both after percutaneous [99-101] and after surgical ablation [40, 96]. In patients with organized arrhythmias after surgical ablation, electrophysiological study shows left re-entry circuits in about half of the cases [36, 65, 96, 102]. These are most frequently related to gaps through the mitral connecting line and/or coronary sinus [65], frequently following surgical cryoablation [40, 65]. Atypical left atrial tachycardias may originate from incomplete isolation of the pulmonary veins [93]. As is the case for recovered conduction across the pulmonary vein line after percutaneous ablation [101, 103, 104], these arrhythmias are highly responsive to repeat percutaneous ablation.

Right relapsing arrhythmias are frequently related to persistent conduction through the cavo-tricuspid connecting line [36, 95, 102]. Another common mechanism of right automatic arrhythmia recurrences is re-entry around ineffectively ablated right atriotomies [95, 96]. More rarely, right arrhythmias recognize a focal origin [96, 102].

Finally, specialized atrial structures such as the Bachman bundle and the crista terminalis, when crossed by surgical lesions may promote flutter circuits through slow conduction, in surgically ablated patients [96].

As to the management of such late recurring arrhythmias, although an attempt with medical treatment and electrical conversion is usually warranted as a first line approach, basically all patients with automatic arrhythmias are good candidates for electrophysiological study and ablation.

Regarding patients with relapsing atrial fibrillation late during follow-up, it has been observed that they are actually amenable to conservative treatment in many instances [22]. In particular, antiarrhythmic medications and DC shock cardioversion as mentioned above are frequently effective when dealing with relapsing atrial fibrillation after an initially successful treatment [22]. Conversely, patients with relapsing atrial fibrillation, especially when permanent, are only occasionally good candidates for percutaneous mapping and re-ablation [36, 65].

In fact, many organized post-ablation arrhythmias are often drug resistant and usually poorly tolerated due to high ventricular rate, and therefore require electrophysiological assessment and ablation [95, 96].

In conclusion, over the last twenty-five years, surgical ablation techniques have been progressively refined. The parallel development of surgical ablation devices has rendered the procedures quicker and simpler and therefore feasible in virtually all clinical contexts. The large-scale adoption of such techniques has raised the issue of post-ablation arrhythmias. Although relapsing atrial fibrillation is generally addressed conservatively, most automatic arrhythmias require electrophysiological assessment and ablation, frequently transseptal.

Completeness of the lesion sets and durable transmurality of the ablations are key to preventing most postoperative dysrhythmias.

References

1. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. Circulation 1998; 98: 946-52.
2. Obadia JF, el Farra M, Bastien OH, Lièvre M, Martelloni Y, Chassignolle JF. Outcome of atrial fibrillation after mitral valve repair. J Thorac Cardiovasc Surg 1997; 114: 179-85.
3. Jessurun ER, van Hemel NM, Kelder JC, et al. Mitral valve surgery and atrial fibrillation: is atrial fibrillation surgery also needed? Eur J Cardiothorac Surg 2000; 17: 530-7.
4. Cox JL, Ad N, Palazzo T. Impact of the maze procedure on the stroke rate in patients with atrial fibrillation. J Thorac Cardiovasc Surg 1999; 118: 833-40.
5. Packer DL, Bardy GH, Worley SJ, et al. Tachycardia-induced cardiomyopathy: a reversible form of left ventricular dysfunction. Am J Cardiol 1986; 57: 563-70.
6. Doukas G, Samani NJ, Alexiou C, et al. Left atrial radiofrequency ablation during mitral valve surgery for continuous atrial fibrillation: a randomized controlled trial. JAMA 2005; 294: 2323-9.
7. Handa N, Schaff HV, Morris JJ, et al Outcome of valve repair and the Cox maze procedure for mitral regurgitation and associated atrial fibrillation. J Thorac Cardiovasc Surg 1999; 118: 628-35.
8. Cox JL, Schuessler RB, Lappas DG, et al. An 8 1,5-year clinical experience with surgery for atrial fibrillation. Ann Surg 1996; 224: 267-75.
9. Sanfilippo AJ, Abascal VM, Sheehan M, et al. Atrial enlargement as a consequence of atrial fibrillation: a prospective echocardiographic study. Circulation 1990; 82: 792-7.
10. Chua LY, Schaff HV, Orszulak TA, Morris JJ. Outcome of mitral valve repair in patients with preoperative atrial fibrillation. J Thorac Cardiovasc Surg 1994; 107: 408-15.
11. Vogt PR, Brunner-LaRocca HP, Rist M, et al. Preoperative predictors of recurrent atrial fibrillation late after successful mitral valve reconstruction. Eur J Cardiothorac Surg 1998; 13: 619-24.
12. Large SR, Hosseinpour AR, Wisbey C, Wells FC. Spontaneous cardioversion and mitral valve repair: a role for surgical cardioversion (Cox-maze)? Eur J Cardiothiorac Surg 1997; 11: 76-80.
13. Alexiou C, Doukas G, Oc M, et al. The effect of preoperative atrial fibrillation on survival following mitral valve repair for degenerative mitral regurgitation. Eur J Cardiothorac Surg 2007; 31: 586-91.
14. Yang SS, Maranhao V, Monheit R, Ablaza SG, Goldberg H. Cardioversion following open-heart valvular surgery. Br Heart J 1996; 28: 309-15.
15. Grigioni F, Avierinos JF, Ling LH, et al. Atrial fibrillation complicating the course of degenerative mitral regurgitation: determinant and long-term out-come. J Am Coll Cardiol 2002; 40: 84-92.
16. Cox JL. Intraoperative options for treating atrial fibrillation associated with mitral valve disease. J Thorac Cardiovasc Surg 2001; 122: 212-5.
17. Brodell GK, Cosgrove D, Schiavone W, Underwood DA, Loop FD. Cardiac rhythm and conduction disturbances in patients undergoing mitral valve surgery. Cleve Clin J Med 1991; 58: 397-9.
18. Kalil RA, Maratia CB, D'Avila A, Ludwig FB. Predictive factors for persistence of atrial fibrillation after mitral valve operation. Ann Thorac Surg 1999; 67: 614-7.
19. Raine D, Dark J, Bourke JP. Effect of mitral valve repair/replacement surgery on atrial arrhythmia behavior. J Heart Valve Dis 2004; 13: 615-21.
20. Crijns HJ, Van Gelder IC, Van der Woude HL, et al. Efficacy of serial electrical cardioversion therapy in patients with chronic atrial fibrillation after valve replacement and implication for surgery to cure atrail fibrillation. Am J Cardiol 1996; 78: 1140-4.

21 Wu TJ, Kerwin WF, Hwang C, Peter CT, Chen PS. Atrial fibrillation: focal activity, re-entry, or both? Heart Rhythm 2004; 1: 117-20.

22. Ad N, Cox JL. Combined mitral valve surgery and the Maze III procedure. Seminar Thorac Cardiovasc Surg 2002; 14: 206-9.
23. Cox JL, Schuessler RB, D'Agostino HJ Jr, et al. The surgical treatment of atrial fibrillation. III. Development of a definitive surgical procedure. J Thorac Cardiovasc Surg 1991; 101: 569-83.
24. Cox JL, Jaquiss RD, Shuessler RB, Boineau JP. Modification of the maze procedure for the treatment of atrial flutter and atrial fibrillation. I. Rationale and surgical results. J Thorac Cardiovasc Surg 1995; 110: 485-95.
25. McCarthy PM, Gillinov AM, Castle L, Chung M, Cosgrove D 3rd. The Cox-Maze procedure: the Cleveland clinic experience. Semin Thorac Cardiovasc Surg 2000; 12: 25-9.
26. Shaff HV, Dearani JA, Daly RC, Orszulak TA, Danielson GK. Cox-Maze procedure for atrial fibrillation: Mayo Clinic experience. Semin Thorac Cardiovasc Surg 2000; 12: 30-7.
27. Kosakai Y, Kawaguchi AT, Isobe F, et al. Modified maze procedure for patients with atrial fibrillation undergoing simultaneous open heart surgery. Circulation 1995; 92 (9 Suppl.): II359-64.
28. Sandoval N, Velasco VM, Orjuela H, et al. Concomitant mitral valve or atrial septal defect surgery and the modified Cox-maze procedure. Am J Cardiol 1996; 77: 591-6.
29. Kawaguchi AT, Kosakai Y, Sasako Y, Eishi K, Nakano K, Kawashima Y. Risks and benefits of combined maze procedure for atrial fibrillation associated with organic heart disease. J Am Coll Cardiol 1996; 28: 985-90.
30. Harada A, Sasaki K, Fukushima T, et al. Atrial activation during chronic atrial fibrillation in patients with isolated mitral valve disease. Ann Thorac Surg 1996; 61: 104-12.
31. Sueda T, Nagata H, Shikata H, et al. Simple left atrial procedure for chronic atrial fibrillation associated with mitral valve disease. Ann Thorac Surg 1996; 62: 1796-800.
32. Sueda T, Nagata H, Orihashi K, et al. Efficacy of a simple left atrial procedure for chronic atrial fibrillation in mitral valve operations. Ann Thorac Surg 1997; 63: 1070-5.
33. Kosakai Y. Treatment of atrial fibrillation using the Maze procedure: the Japanese experience. Semin Thorac Cardiovasc Surg 2000; 12: 44-52.
34. Gillinov AM, Blackstone EH, McCarthy PM. Atrial fibrillation: current surgical option and their assessment. Ann Thorac Surg 2000; 74: 2210-7.
35. Sie HT, Beukema WP, Elvan A, Ramdat Misier AR. Long term results of irrigated radiofrequency modified maze procedure in 200 patients with concomitant cardiac surgery: six years experience. Ann Thorac Surg 2004; 77: 512-17.
36. Benussi S, Pappone C, Nascimbene S, et al. A simple way to treat atrial fibrillation during mitral valve surgery: the epicardial radiofrequency approach. Eur J Cardiothorac Surg 2000; 17: 524-9.
37. Melo J, Adragao P, Neves J, et al. Endocardial and epicardial radiofrequency ablation in the treatment of atrial fibrillation with a new intra-operative device. Eur J Cardiothorac Surg 2000; 18: 182-6.
38. Sueda T, Imai K, Ishii O, Orihashi K, Watari M, Okada K. Midterm result of pulmonary vein isolation for elimination of chronic atrial fibrillation. Ann Thorac Surg 2005; 79: 521-5.

39. Gillinov AM, McCarthy PM, Blackstone EH, et al. Surgical ablation of atrial fibrillation with bipolar radiofrequency as the primary modality. J Thorac Cardiovasc Surg 2005; 129: 1322-9.
40. Gaita F, Riccardi R, Caponi D, et al. Linear cryoablation of the left atrium versus pulmonary vein cryoisolation in patients with permanent atrial fibrillation and valvular heart disease: correlation of electroanatomic mapping and long-term clinical results. Circulation 2005; 111: 136-42.
41. Benussi S, Nascimbene S, Galanti A, et al. Complete left atrial ablation with bipolar radiofrequency. Eur J Cardiothorac Surg 2008; 33: 590-5.
42. Barnett SD, Ad N. Surgical ablation as treatment for elimination of atrial fibrillation: a meta-analysis. J Thorac Cardiovasc Surg 2006; 131: 1029-35.
43. Melo JQ, Neves J, Adragao P, et al. When and how to report results of surgey on atrial fibrillation. Eur J Cardiothorac Surg 1997; 12: 739-45.
44. Kondo N, Takahashi K, Minakawa M, Daitoku K. Left atrial maze procedure: a useful addition to other corrective operations. Ann Thorac Surg 2003; 75: 1490-4.
45. Kalil RA, Lima GG, Leiria TL, et al. Simple surgical isolation of pulmonary veins for treating secondary atrial fibrillation in mitral valve disease. Ann Thorac Surg 2002; 73: 1169-73.
46. Ruchat P, Schlapfleer J, Fromer M, et al. Atrial fibrillation inhibition by subepicardial radiofrequency ablation in a sheep model (Abstract). Abstract Book of the 12th Annual Meeting of the EACTS 1998: 434.
47. Benussi S, Nascimbene S, Agricola E, et al. Surgical ablation of atrial fibrillation using the epicardial radiofrequency approach: mid-term results and risk analysis. Ann Thorac Surg 2002; 74: 1050-7.
48. Benussi S. Treatment of atrial fibrillation. Eur J Cardiothorac Surg 2004; 26 (Suppl. 1): S39-41.
49. Maessen JG, Nijs JF, Smeets JL, Vainer J, Mochtar B. Beating-heart surgical treatment of atrial fibrillation with microwave ablation. Ann Thorac Surg 2002; 74: S1307-11.
50. Saltman AE, Rosenthal LS, Francalancia NA, Lahey SJ. A completely endoscopic approach to microwave ablation for atrial fibrillation. Heart Surg Forum 2003; 6: E38-41.
51. Reade CC, Johnson JO, Bolotin G, et al. Combining robotic mitral valve repair and microwave atrial fibrillation ablation: techniques and initial results. Ann Thorac Surg 2005; 79: 480-4.
52. Doll N, Kiaii BB, Fabricius AM, et al. Intraoperative left atrial ablation (for atrial fibrillation) using a new argon cryocatheter: early clinical experience. Ann Thorac Surg 2003; 76: 1711-5.
53. Mack CA, Milla F, Ko W, et al. Surgical treatment of atrial fibrillation using argon-based cryoablation during concomitant cardiac procedures. Circulation 2005; 112 (9 Suppl.): I1-6.
54. Ninet J, Roques X, Seitelberger R, et al. Surgical ablation of atrial fibrillation with off-pump, epicardial, high-intensity focused ultrasound: results of a multicenter trial. J Thorac Cardiovasc Surg 2005; 130: 803-9.
55. Doll N, Borger MA, Fabricius A, et al. Esophageal perforation during left atrial radiofrequency ablation: Is the risk too high? J Thorac Cardiovasc Surg 2003; 125: 836-42.
56. Santiago T, Melo J, Gouveia RH, et al. Epicardial radiofrequency applications: in vitro and in vivo studies on human atrial myocardium. Eur J Cardiothorac Surg 2003; 24: 481-6.
57. Colangelo N, Benussi S, Nascimbene S, et al. Cardiopulmonary bypass strategy during concomitant surgical treatment of mitral valve disease and atrial fibrillation. Perfusion 2003; 18: 19-24.
58. Gillinov AM, McCarthy PM. Atricure bipolar radiofrequency clamp for intraoperative ablation of atrial fibrillation. Ann Thorac Surg 2002; 74: 2165-8.
59. Prasad SM, Maniar HS, Diodato MD, Schuessler RB, Damiano RJ Jr. Physiological consequences of bipolar radiofrequency energy on the atria and pulmonary veins: a chronic animal study. Ann Thorac Surg 2003; 76: 836-41.
60. Gaynor SL, Diodato MD, Prasad SM, et al. A prospective, single-center clinical trial of a modified Cox maze procedure with bipolar radiofrequency ablation. J Thorac Cardiovasc Surg 2004; 128: 535-42.
61. Benussi S, Nascimbene S, Calori G, et al. Surgical ablation of atrial fibrillation with a novel bipolar radiofrequency device. J Thorac Cardiovasc Surg 2005; 130: 491-7.
62. Magnano AR, Argenziano M, Dizon JM, et al. Mechanisms of atrial tachyarrhythmias following surgical atrial fibrillation ablation. J Cardiovasc Electrophysiol 2006; 17: 366-73.
63. Bruins P, te Velthuis H, Yazdanbakhsh AP, et al. Activation of the complement system during and after cardiopulmonary bypass surgery: postsurgery activation involves C-reactive protein and is associated with postoperative arrhythmia. Circulation 1997; 96: 3542-8.
64. Chung MK, Martin DO, Sprecher D, et al. C-reactive protein elevation in patients with atrial arrhythmias: inflammatory mechanisms and and persistence of atrial fibrillation. Circulation 2001; 104: 2886-91.
65. Ishii Y, Gleva MJ, Gamache MC, et al. Atrial tachyarrhythmias after the Maze procedure. Circulation 2004; 110 (Suppl. I): II164-8.
66. Sinno H, Derakhchan K, Libersan D, Merhi Y, Leung TK, Nattel S. Atrial ischemia promotes atrial fibrillation in dogs. Circulation 2003; 107: 1930-6.
67. Cox JL. A perspective of postoperative atrial fibrillation in cardiac operations. Ann Thorac Surg 1993; 56: 405-9.
68. Mohr FW, Fabricius AM, Falk V, et al. Curative treatment of atrial fibrillation with intraoperative radiofrequency ablation: short-terms and midterms results. J Thorac Cardiovasc Surg 2002; 123: 919-27.
69. Corradi D, Callegari S, Benussi S, et al. Regional left atrial interstitial remodelling in patients with chronic atrial fibrillation undergoing mitral-valve surgery. Virch Arch 2004; 445: 498-505.
70. Corradi D, Callegari S, Benussi S, et al. Myocyte changes and their left atrial distribution in patients with chronic atrial fibrillation related to mitral valve disease. Hum Pathol 2005; 36: 1080-9.
71. Schwartzman D, Parizhskaya M, Devine WA. Linear ablation using an irrigated electrode electrophysiologic and histologic lesion evolution comparison with ablation utilizing a non-irrigated electrode. J Interv Card Electrophysiol 2001; 5: 17-26.
72. Bugge E, Nicholson IA, Thomas SP. Comparison of bipolar and unipolar radiofrequency in an in vivo experimental model. Eur J Cardiothorac Surg 2005; 28: 76-80.
73. Cox JL, Boineau JP, Schuessler RB, Kater KM, Lappas DG. Five-year experience with the maze procedure for atrial fibrillation. Ann Thorac Surg 1993; 56: 814-24.
74. Akpinar B, Gauden M, Sagbas E, et al. Combined radiofrequency modified maze and mitral valve procedure through a port access approach: early and mid-term results. Eur J Cardiothorac Surg 2003; 24: 223-30.
75. Geidel S, Lass M, Boczor S, et al. Surgical treatment of permanent atrial fibrillation during heart valve surgery. Interact Cardiovasc Thorac Surg 2003; 2: 160-5.
76. Ad N, Barnett S, Lefrak EA, et al. Impact of follow-up on the success rate of the cryosurgical maze procedure in patients with rheumatic heart disease and enlarge atria. J Thorac Cardiovasc Surg 2006; 131: 1073-9.

77. Albåge A, Lindblom D, Insulander P, Kennebäck G. Electrophysiological evaluation of the sinus node and the cardiac conduction system following the maze procedure for atrial fibrillation. Pacing Clin Electrophysiol 2004; 27: 194-203.
78. Elvan A, Wylie K, Zipes DP. Pacing-induced chronic atrial fibrillation impairs sinus node function in dogs. Electrophysiological remodelling. Circulation 1996; 94: 2953-60.
79. Schuetz A, Schulze CJ, Sarvanakis KK, et al. Surgical treatment of permanent atrial fibrillation using microwave energy ablation: a prospective randomised clinical trial. Eur J Cardiothorac Surg 2003; 24: 475-80.
80. Knaut M, Spitzer SG, Karolyi L, et al. Intraoperative microwave ablation for curative treatment of atrial fibrillation in open heart surrgey-the MICRO-STAF and MICRO-PASS pilot trial. MICROwave application in surgical treatment of atrial fibrillation. MICROwave Application for the Treatment of Atrial fibrillation in Bypass-surgery. J Thorac Cardiovas Surg 1999; 47 (Suppl. 3): 379-84.
81. Madrid AH, Bueno MG, Rebollo JM, et al. Use of irbesartan to mantain sinus rhythm in patients with long-lasting persistent atrial fibrillation: a prospective and randomised study. Circulation 2002; 106: 331-6.
82. Chiappini B, Leone O, Bracchetti G, Marinelli G. The role of corticosteroid therapy following surgery for atrial fibrillation. J Card Surg 2004; 19: 232-4.
83. Shemin RJ, Cox JL, Gillinov AM, Blackstone EH, Bridges CR; Workforce on Evidence-Based Surgery of the Society of Thoracic Surgeons. Guidelines for reporting data and outcomes for the surgical treatment of atrial fibrillation. Ann Thorac Surg 2007; 83: 1225-30.
84. Voeller RK, Bailey MS, Zierer A, et al. Surgical outcomes following the Cox-Maze procedure: the importance of isolating posterior left atrium. Oral communication at the 87th annual meeting of the American Association for Thoracic Surgery.
85. Patterson E, Po SS, Scherlag BJ, et al. Triggered firing in pulmonary veins initiated by in vitro autonomic nerve stimulation. Heart Rhythm 2005; 2: 624-31.
86. Chevalier P, Tabib A, Meyronnet D, et al. Quantitative study of nerves of the human left atrium. Heart Rhythm 2005; 2: 518-22.
87. Stulak JM, Sundt TM 3rd, Dearani JA, Daly RC, Orsulak TA, Schaff HV. Ten-year experience with the Cox-maze procedure for atrial fibrillation: how do we define success? Ann Thorac Surg 2007; 83: 1319-24.
88. Kobayashi J, Kosakai Y, Nakano K, Sasako Y, Eishi K, Yamamoto F. Improved success rate of the maze procedure in mitral valve disease by new criteria for patients' selection. Eur J Cardiothorac Surg 1998; 13: 247-52.
89. Baek MJ, Na CY, Oh SS, et al. Surgical treatment of chronic atrial fibrillation combined with rheumatic mitral valve disease:effects of the cryo-maze procedure and predictors for late recurrence. Eur J Cardiothoracic Surg 2006; 30: 728-36.
90. Imai K, Sueda T, Orihashi K, Watari M, Matsuura Y. Clinical analysis of results of a simple left atrial procedure for chronic atrial fibrillation. Ann Thorac Surg 2001; 71: 577-81.
91. Gaynor SL, Schuessler RB, Bailey MS, et al. Surgical treatment of atrial fibrillation: Predictors of late recurrence. J Thorac Cardiovasc Surg 2005; 129: 104-11.
92. Thomas SP, Nunn GR, Nicholson AI, et al. Mechanism, localization and cure of atrial arrhythmias occurring after a new intraoperative endocardial radiofrequency ablation procedure for atrial fibrillation. J Am Coll Cardiol 2000; 35: 442-50.
93. Todd DM, Skanes AC, Guiraudon C, et al. Role of the posterior left atrium and pulmonary veins in human lone atrial fibrillation: electrophysiological and pathological data from patients undergoing atrial fibrillation surgery. Circulation 2003; 108: 3108-14.
94. Deneke T, Khargi K, Grewe PH, et al. Left atrial versus bi-atrial Maze operation using intraoperatively cooled-tip radiofrequency ablation in patients undergoing open-heart surgery: safety and efficacy. J Am Coll Cardiol 2002; 39: 1644-50.
95. Usui A, Inden Y, Mizutani S, et al. Repetitive atrial flutter as a complication of the left-sided simple maze procedure. Ann Thorac Surg 2002; 73: 1457-9.
96. McElderry HT, McGiffin DC, Plumb VJ, et al. Proarrhythmic aspects of atrial fibrillation surgery: mechanism of postoperative macroreentrant tachycardias. Circulation 2008; 117: 155-62.
97. Graffigna A, Pagani F, Minzioni G, Salerno J, Viganò M. Left atrial isolation associated with mitral valve operations. Ann Thorac Surg 1992; 54: 1093-7.
98. Cox JL. Atrial fibrillation II: rationale for surgical treatment. J Thorac Cardiovasc Surg 2003; 126: 1693-9.
99. Duru F, Hindricks G, Kottkamp H. Atypical left atrial flutter after intraoperative radiofrequency ablation of chronic atrial fibrillation: successful ablation using three-dimensional electroanatomic mapping. J Cardiovasc Electrophysiol 2001; 12: 602-5.
100. Mainigi SK, Sauer WH, Cooper JM, et al. Incidence and predictors of very late recurrence of atrial fibrillation after ablation. J Cardiovasc Electrophysiol 2006; 18: 69-74.
101. Mesas CE, Pappone C, Lang CC, et al. Left atrial tachycardia after circumferential pulmonary vein ablation for atrial fibrillation: electroanatomic characterization and treatment. J Am Coll Cardiol 2004; 44: 1071-9.
102. Kobza R, Kottkamp H, Dorszewski A, et al. Stable secondary arrhythmias late after intraoperative radiofrequency ablation of atrial fibrillation: incidence, mechanism, and treatment. J Cardiovasc Electrophysiol 2004; 15: 1246-49.
103. Cheema A, Dong J, Dalal D, et al. Incidence and time course of early recovery of pulmonary vein conduction after catheter ablation of atrial fibrillation. J Cardiovasc Electrophysiol 2007; 18: 387-91.
104. Ouyang F, Antz M, Ernst S, et al. Recovered pulmonary vein conduction as a dominant factor for recurrent atrial tachyarrhythmias after complete circular isolation of the pulmonary veins. Circulation 2005; 111: 127-35.